

The CBHSQ Report

Short Report

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EMERGENCY DEPARTMENT VISITS INVOLVING BUPRENORPHINE

AUTHORS

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INTRODUCTION

Buprenorphine is a medication used to treat opioid addiction. A properly prescribed dose of buprenorphine can help opioid-addicted individuals to stop misusing opioids without experiencing withdrawal symptoms. Although buprenorphine is itself an opioid, and can thus have the same effects as other opioids (e.g., heroin, oxycodone), its maximum effects are less than those of other opioids.¹ Therefore, with buprenorphine there is a decreased risk of abuse, addiction, and side effects compared with other opioids. Buprenorphine was approved for use in the United States for the treatment of opioid dependence in 2002² and is primarily available in two formulations: one that contains only buprenorphine (Subutex®) and one that contains buprenorphine and naloxone (Suboxone®).^{3,4} Naloxone reverses opioid overdoses and prevents buprenorphine from being misused by injection.¹ Most of the buprenorphine used for treatment in the United States is the buprenorphine-naloxone formulation, which can be prescribed by certified physicians.⁵ In this report, “buprenorphine” refers to both formulations of the drug. Availability of buprenorphine is less restricted than other treatments for opioid dependence, such as methadone, which can only be administered in specialized clinics. Although this availability can increase access to treatment, it can also increase the potential for diversion and misuse by those who are not opioid dependent.⁶ Such use can lead to buprenorphine dependence or abuse.²

Harmful consequences can occur even when buprenorphine is taken as prescribed by a physician. If used by an individual who is dependent on large doses of opioids, buprenorphine can block the effect of other opioids and bring on withdrawal symptoms.¹ Although these symptoms are not usually severe, emergency medical care may be required to relieve symptoms. Additionally, adverse reactions or drug interactions may occur.¹ The potential for these consequences coupled with increasing availability call for careful monitoring of buprenorphine-related emergency department (ED) visits.

This issue of *The DAWN Report* discusses the trends and characteristics of ED visits involving buprenorphine. The Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related ED visits in the United States and can be used to track buprenorphine-related ED visits. To be a DAWN case, an ED visit must have involved a drug, either as the direct cause of the visit or as a contributing factor.



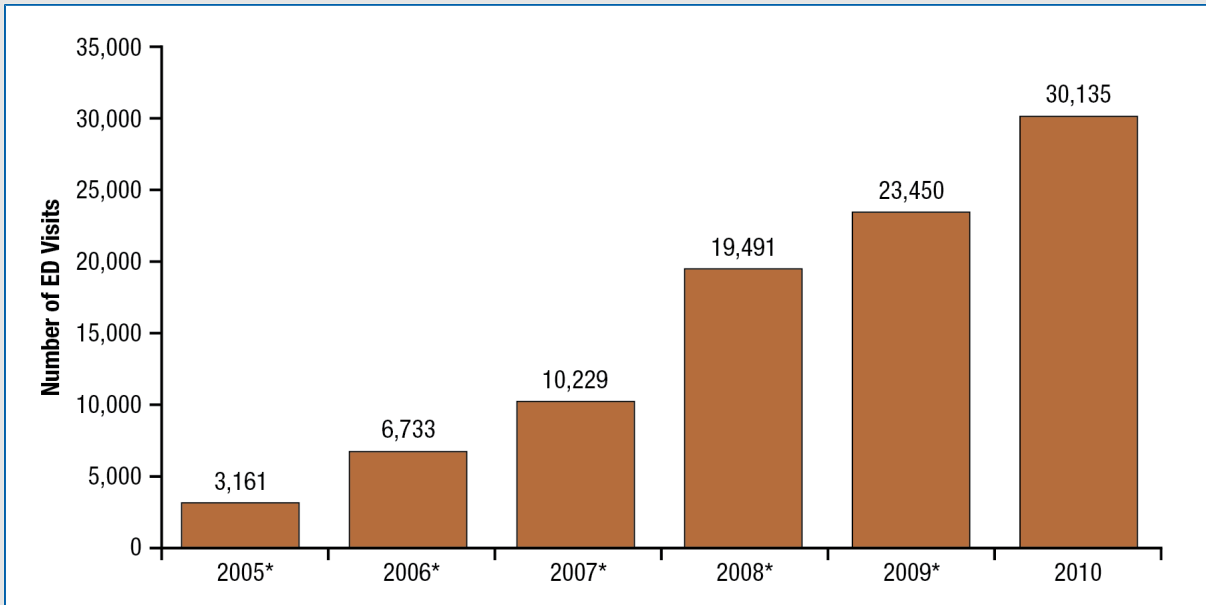
In Brief

- Emergency department (ED) visits involving buprenorphine increased substantially from 3,161 in 2005 to 30,135 visits in 2010, as availability of the drug increased
- In 2010, most buprenorphine-related ED visits were classified as nonmedical use of pharmaceuticals (52 percent, or 15,778 visits), followed by patients seeking detoxification or substance abuse treatment (24 percent, or 7,372 visits) and adverse reactions (13 percent, or 4,017 visits)
- Buprenorphine-related ED visits involving nonmedical use of pharmaceuticals increased 255 percent from 4,440 visits in 2006 to 15,778 visits in 2010
- Additional drugs were involved in 59 percent of buprenorphine-related ED visits involving nonmedical use of pharmaceuticals in 2010

OVERVIEW

ED visits involving buprenorphine increased substantially from 3,161 in 2005 to 30,135 visits in 2010 (Figure 1). This trend likely reflects the increased availability of buprenorphine after the Food and Drug Administration approved its use for treatment of opioid dependence in 2002,² and the increasing number of physicians who subsequently became certified to prescribe it.⁷ At the close of 2005, there were 5,656 physicians certified to prescribe buprenorphine products for addiction treatment. By the end of 2010, the number of certified physicians had increased to 18,582, representing a more than threefold increase in certified buprenorphine prescribers.⁸

Figure 1. Emergency Department (ED) Visits Involving Buprenorphine: 2005 to 2010



* The estimate was statistically significantly different from the estimate for 2010 at the .05 level.

Source: 2005 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

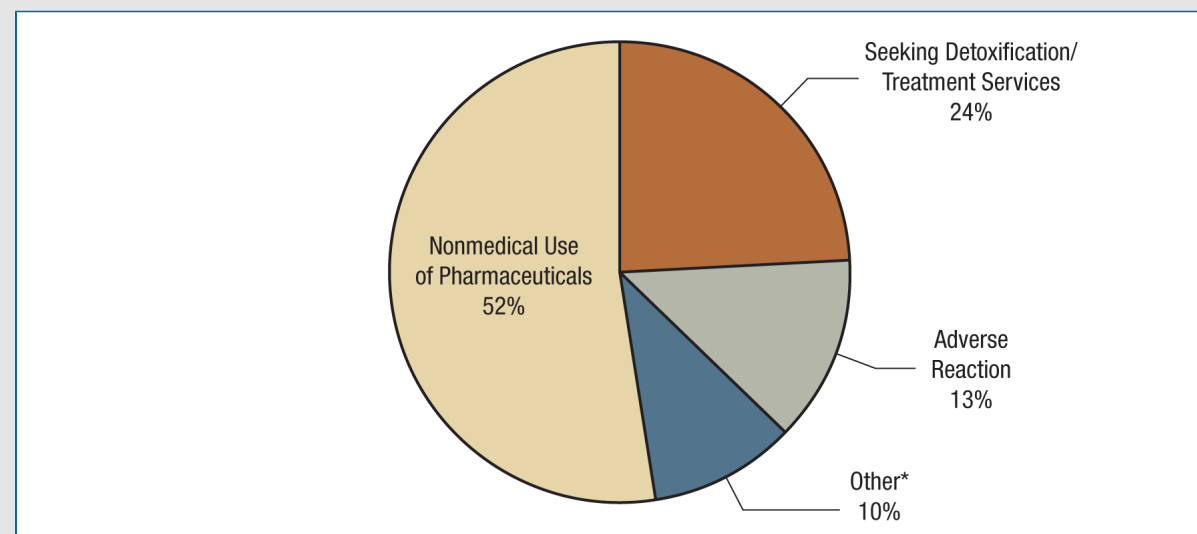
Increases in the availability of buprenorphine products are also reflected in the number of patients receiving prescriptions for buprenorphine products. For example, in 2005, approximately 100,000 individual patients had received a buprenorphine prescription. By 2010, more than 800,000 patients had received a prescription for buprenorphine products—an eightfold increase.⁹

A number of these certified physicians were affiliated with substance abuse treatment facilities, some of which offered buprenorphine as a treatment option. The number of substance abuse treatment facilities offering buprenorphine treatment increased 231 percent, from 741 facilities in 2003 to 2,451 facilities in 2010.^{10,11}

Most buprenorphine-related ED visits fell into one of three types of visits: patients seeking detoxification or substance abuse treatment,¹² adverse reactions to medications,¹³ or nonmedical use of pharmaceuticals. Nonmedical use includes taking more than the prescribed dose of a prescription medication or more than the recommended dose of an over-the-counter (OTC) medication or supplement, taking a prescription medication prescribed for another individual, being deliberately poisoned with a pharmaceutical by another person, or misusing or abusing a prescription medication, an OTC medication, or a dietary supplement.

In 2010, 52 percent of buprenorphine-related ED visits involved nonmedical use of pharmaceuticals, 24 percent involved patients seeking detoxification or substance abuse treatment, and 13 percent involved adverse reactions to medications (Figure 2). The remainder of this report focuses on each of these types of visits, and includes data on trends (where possible) and characteristics of visits in 2010.

Figure 2. Emergency Department (ED) Visits Involving Buprenorphine, by Type of Visit: 2010



* Other types of visits include accidental ingestion and suicide attempts. Because of rounding, percentages do not add to 100.

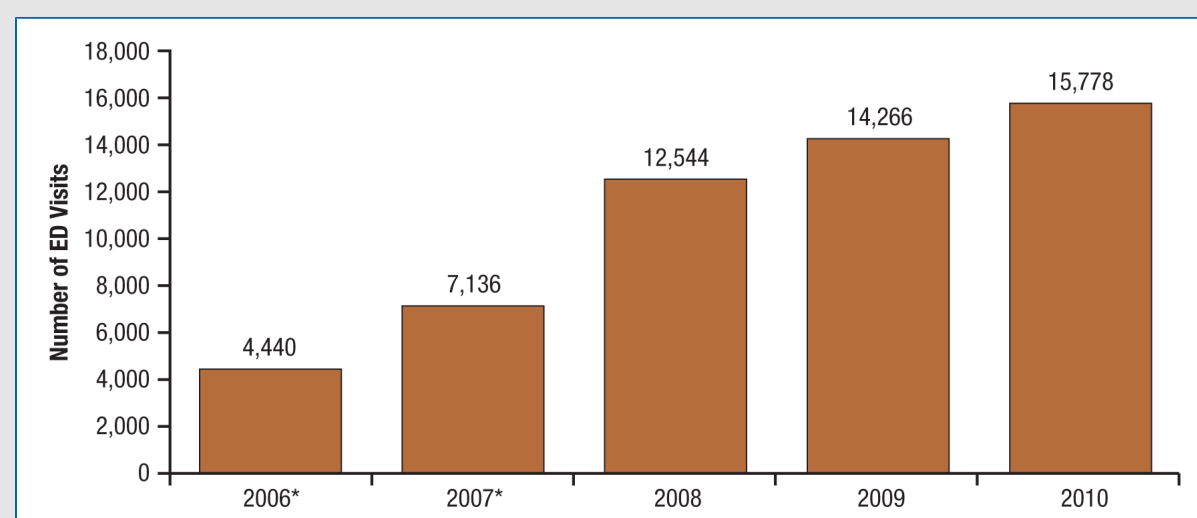
Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

VISITS INVOLVING NONMEDICAL USE OF PHARMACEUTICALS

Trends

Buprenorphine-related ED visits involving nonmedical use of pharmaceuticals increased 255 percent from 4,440 visits in 2006 to 15,778 visits in 2010 (Figure 3); estimates for 2005 were suppressed due to low precision. Although visits appeared to increase between 2008 and 2010 and between 2009 and 2010, the changes were not statistically significant.

Figure 3. Buprenorphine-Related Emergency Department (ED) Visits Involving Nonmedical Use of Pharmaceuticals: 2006 to 2010



* The estimate was statistically significantly different from the estimate for 2010 at the .05 level.

Source: 2006 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Demographic Characteristics

In 2010, most buprenorphine-related ED visits involving nonmedical use of pharmaceuticals involved male patients (66 percent). Patients aged 26 to 34 accounted for the highest proportion of visits for nonmedical use (38 percent), followed by patients aged 18 to 25 (24 percent), aged 35 to 44 (15 percent), and aged 45 to 54 (13 percent).

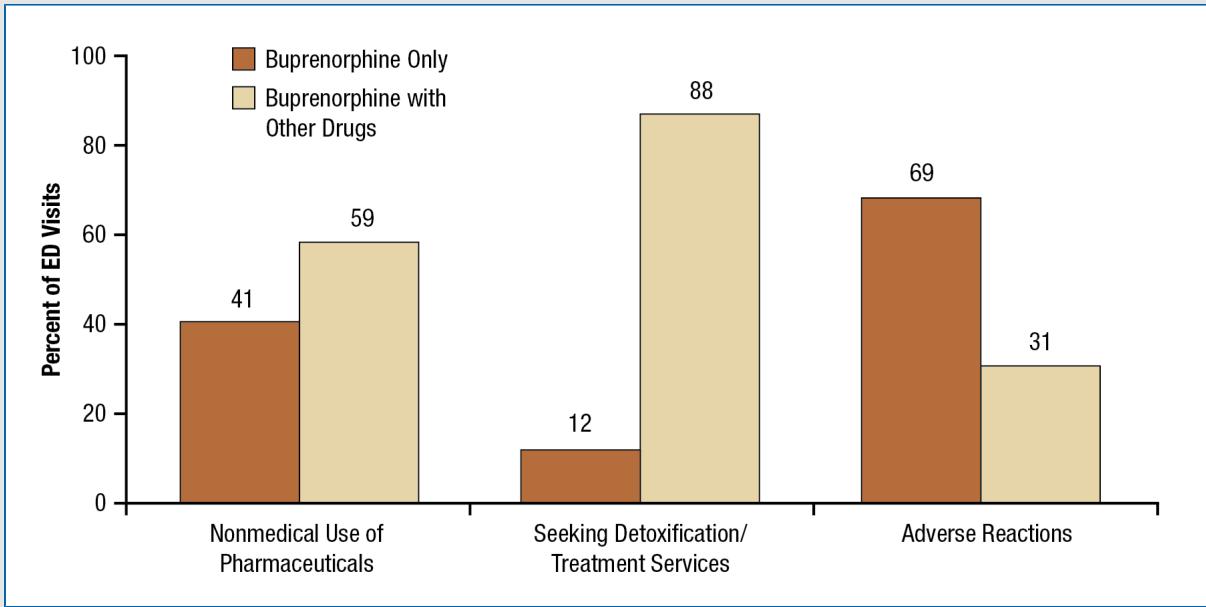
Drug Combinations with Buprenorphine

To understand the role of buprenorphine or any other drug involved in a drug-related ED visit, it is important to differentiate between the visits that involved a single drug and those where multiple drugs were involved. When a single drug is involved, the ED visit can be attributed to that drug (whether it was the direct cause of the visit or a contributing factor), but when multiple drugs are involved, the visit cannot be attributed to a single drug.

Furthermore, there are several different reasons why nonmedical use of pharmaceuticals may occur, and when multiple drugs are involved, they may have been taken for different reasons. This issue is particularly relevant for buprenorphine because it is both an opioid and a treatment for opioid dependence. The buprenorphine in these visits may have been misused or abused, either for psychoactive effects or in an attempt to self-treat for opioid dependence (without a prescription),¹⁴ or the buprenorphine may have been used appropriately but mixed with other drugs that were being abused or misused.

In 2010, 41 percent of buprenorphine-related ED visits involving nonmedical use of pharmaceuticals involved buprenorphine only (Figure 4). In the remaining 59 percent of these visits, another drug was involved. More specifically, pharmaceuticals were combined with buprenorphine in 43 percent of visits (Table 1). The most common types of pharmaceuticals were benzodiazepines, which are commonly prescribed to treat anxiety and insomnia (27 percent of visits). A specific benzodiazepine, alprazolam (Xanax®), was combined with buprenorphine in 12 percent of visits. Narcotic pain relievers other than buprenorphine were involved in 12 percent of visits; more specifically, 6 percent of visits involved the narcotic pain reliever oxycodone, and 3 percent of visits involved an unspecified opiate.

Figure 4. Drug Combinations among Emergency Department (ED) Visits Involving Buprenorphine, by Type of Visit: 2010



Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Table 1. Selected Drug Combinations among Emergency Department (ED) Visits Involving Buprenorphine, by Type of Visit: 2010*

	Number of ED Visits: Nonmedical Use of Pharma- ceuticals	Percent of ED Visits: Nonmedical Use of Pharma- ceuticals	Number of ED Visits: Seeking Detoxi- fication/ Treatment Services	Percent of ED Visits: Seeking Detoxi- fication/ Treatment Services	Number of ED Visits: Adverse Reactions	Percent of ED Visits: Adverse Reactions
Total ED Visits	15,778	100	7,372	100	4,017	100
Combinations with						
Other Pharmaceuticals	6,840	43	6,100	83	1,235	31
Other Narcotic Pain Relievers	1,900	12	4,300	58	**	**
Oxycodone	991	6	4,195	57	**	**
Anti-Anxiety and Insomnia Medications	4,269	27	2,255	31	**	**
Benzodiazepines	4,214	27	2,239	30	**	**
Alprazolam	1,906	12	**	**	**	**
Combinations with Illicit Drugs	4,262	27	**	**	N/A	N/A
Marijuana	1,790	11	**	**	N/A	N/A
Heroin	1,366	9	**	**	N/A	N/A
Cocaine	1,237	8	**	**	N/A	N/A
Combinations with Alcohol	1,691	11	**	**	**	**

* Because multiple drugs may be involved in each visit, estimates of visits by drug may add to more than the total, and percentages may add to more than 100 percent.

**Not shown due to low statistical precision.

Note: N/A = Not applicable; in DAWN, visits involving illicit drugs are not categorized as adverse reactions.

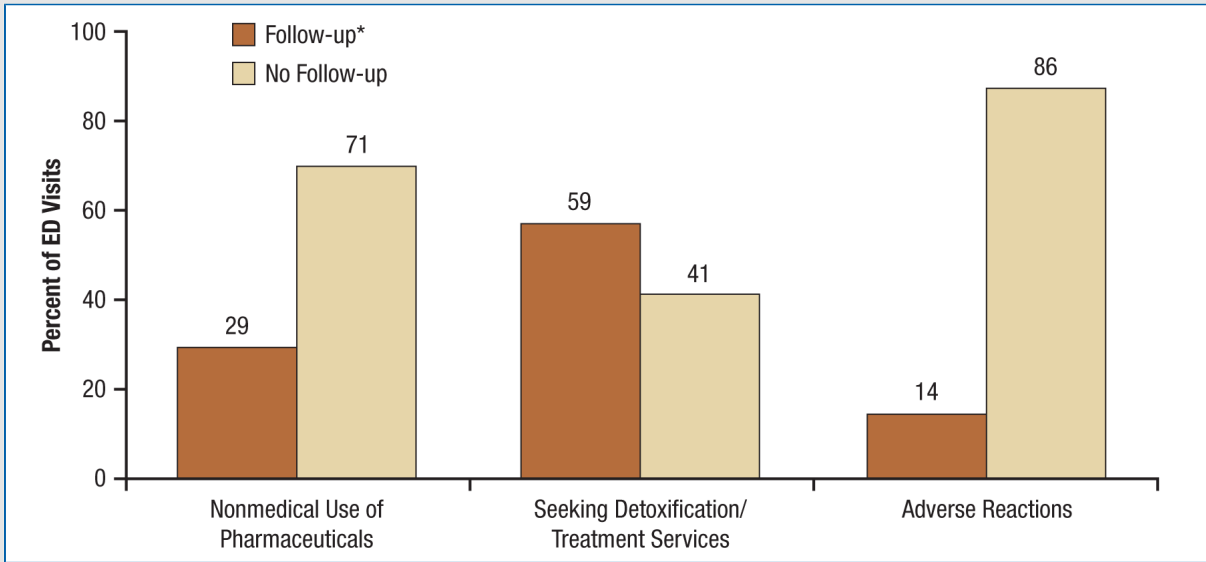
Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Illicit drugs were involved in 27 percent of buprenorphine-related visits, especially marijuana (11 percent of visits), heroin (9 percent), and cocaine (8 percent). Alcohol was involved in 11 percent of visits.

Disposition of ED Visits

There was evidence of some type of follow-up in 29 percent of buprenorphine-related ED visits involving nonmedical use of pharmaceuticals in 2010: the patient was admitted to the hospital, transferred to another facility, or discharged with a referral to detoxification or substance abuse treatment (Figure 5). For this analysis, it was not possible to determine what precipitating health event led to each ED visit (i.e., whether it was an opioid overdose, withdrawal triggered by the buprenorphine, or a situation, such as a motor vehicle crash, in which drugs contributed to the ED visit but were not the direct cause).

Figure 5. Emergency Department (ED) Visits Involving Buprenorphine Resulting in Follow-up or No Follow-up, by Type of Visit: 2010



* The patient was admitted to the hospital, transferred to another facility, or discharged with a referral to detoxification or substance abuse treatment.

Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

VISITS INVOLVING PATIENTS SEEKING DETOXIFICATION

Trends

No significant increase in overall visits occurred from 2009 to 2010 for buprenorphine-related visits involving patients seeking detoxification or substance abuse treatment. Estimates for previous years were suppressed due to low precision.

Demographic Characteristics

In 2010, of the 7,372 buprenorphine-related visits in which patients were seeking detoxification, 5,743 (78 percent) were aged 21 or older. In 2009, the only year in which statistically reliable estimates by gender could be produced, 82 percent involved male patients.

Drug Combinations with Buprenorphine

Among buprenorphine-related visits involving patients seeking detoxification in 2010, buprenorphine was used in combination with other drugs in 88 percent of visits (Figure 4). In 83 percent of visits, pharmaceuticals were combined with buprenorphine (Table 1). Other narcotic pain relievers were combined with buprenorphine in 58 percent of visits, and the narcotic pain reliever oxycodone was specified in 57 percent of visits. The finding that both oxycodone and buprenorphine were involved in more than half of visits for patients seeking detoxification or substance abuse treatment raises the possibility that some of these patients may have been attempting to self-treat oxycodone dependence using buprenorphine that was not prescribed for them.¹⁴

Disposition of ED Visits

There was evidence of some type of follow-up in 59 percent of ED visits involving patients seeking detoxification in 2010; however, in 41 percent of visits, the patient was discharged from the ED without any evidence of their request for detoxification or substance abuse treatment being met (Figure 5).

VISITS INVOLVING ADVERSE REACTIONS

Trends

Buprenorphine-related ED visits involving adverse reactions increased from 649 visits in 2005 to 4,017 visits in 2010 (Figure 6). Because visits appeared to fluctuate over time and estimates for 2006 were suppressed due to low precision, the trend pattern is difficult to interpret.

Demographic Characteristics

Males accounted for two thirds (67 percent) of visits involving adverse reactions in 2010, and patients aged 26 to 34 accounted for the highest proportion of visits (30 percent).

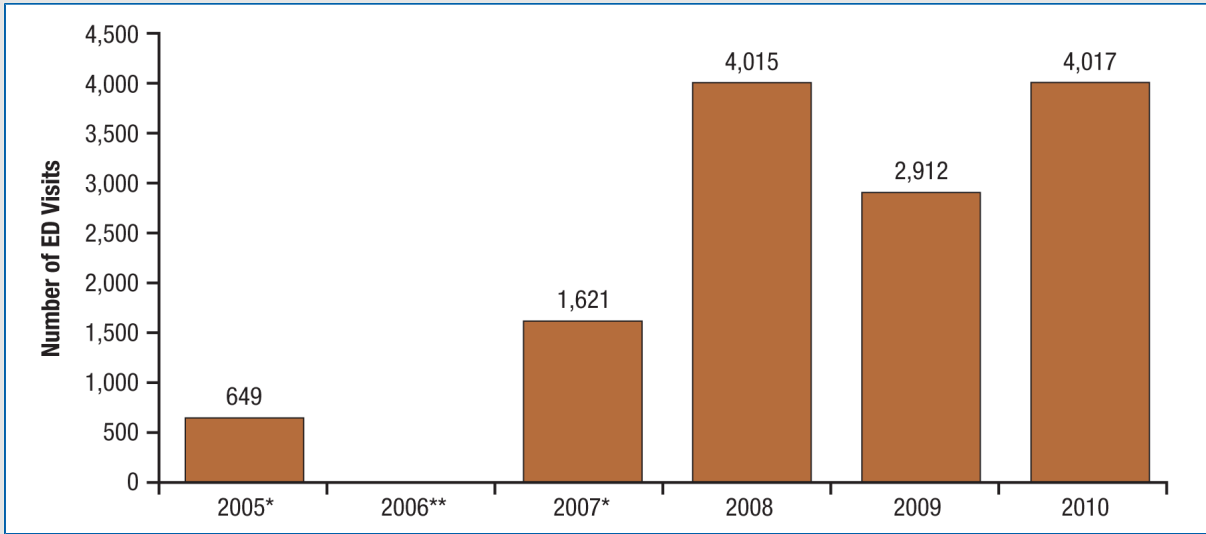
Drug Combinations with Buprenorphine

Among buprenorphine-related visits involving adverse reactions in 2010, most (69 percent) involved buprenorphine only (Figure 4). An estimated 31 percent of visits involved other pharmaceuticals combined with buprenorphine (Table 1).

Disposition of ED Visits

There was evidence of some type of follow-up in only 14 percent of ED visits involving adverse reactions in 2010; therefore, most patients (86 percent) were discharged from the ED without follow-up (Figure 5).

Figure 6. Buprenorphine-Related Emergency Department (ED) Visits Involving Adverse Reactions: 2005 to 2010



* The estimate was statistically significantly different from the estimate for 2010 at the .05 level.
** The estimate for 2006 was not shown due to low statistical precision.
Source: 2005 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

DISCUSSION

Findings in this report show significant growth in the number of ED visits involving buprenorphine at the same time that there has been an increase in its availability for treatment of opioid dependence. These data show that buprenorphine is sometimes used nonmedically, resulting in health events that require acute treatment in the ED. Buprenorphine use can be risky for individuals who are not opioid dependent because its effects are similar to other opioids (although usually more mild), leading to injuries and other health consequences.¹ Additionally, dangerous effects can occur if buprenorphine is combined with certain other drugs, including benzodiazepines.¹

With careful management, buprenorphine treatment for opioid dependence can be safe and more accessible than other forms of treatment. For patients who may be attempting to self-treat opioid dependence using buprenorphine without a prescription, expanding access to treatment and putting these patients in the care of a certified physician may help reduce the nonmedical use of buprenorphine and subsequent ED visits.¹⁴ Certified physicians can be located at http://buprenorphine.samhsa.gov/bwns_locator/. Physicians prescribing buprenorphine can manage the dose needed to avoid severe opioid withdrawal symptoms.³ However, if a patient arrives in the ED experiencing such symptoms, medical staff can assess withdrawal symptoms, provide treatment as necessary, and educate patients about symptoms that can be expected to diminish over time.³

END NOTES

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4. Both Subutex® (buprenorphine) and Suboxone® (buprenorphine and naloxone) are products of Reckitt-Benckiser Pharmaceuticals, Inc. Reckitt-Benckiser discontinued production of Subutex®, but generic versions may still be available from other manufacturers. In August 2010, Reckitt-Benckiser received FDA approval to release a new form of Suboxone®: a strip of film that is placed under the tongue to dissolve. In September 2012, Reckitt Benckiser Pharmaceuticals, Inc., notified the FDA that the company is voluntarily discontinuing the supply of Suboxone® tablets in the United States because of increasing concerns about pediatric exposure. More information can be found at <http://www.suboxone.com>.
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12. Seeking detoxification includes nonemergency requests for admission for detoxification and visits to obtain medical clearance before entry to a detoxification program as well as acute emergencies in which an individual is experiencing withdrawal symptoms and seeking detoxification. Because detoxification may be sought through other avenues (e.g., direct admission to a hospital, services provided through private clinics, entry into programs outside the community), the overall demand for detoxification services is most likely higher than suggested by DAWN estimates.
13. Adverse reactions are defined as ED visits in which an adverse health consequence results from taking prescription drugs, OTC medications, or dietary supplements as prescribed or recommended. A visit is not included in this category if an illicit drug is involved.
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SUGGESTED CITATION

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SUMMARY

Background: Buprenorphine is a medication used to treat opioid addiction. A properly prescribed dose of buprenorphine can help opioid-addicted individuals to stop misusing opioids without experiencing withdrawal symptoms. Although buprenorphine is itself an opioid, and can thus have the same effects as other opioids (e.g., heroin, oxycodone), its maximum effects are less than those of other opioids. Therefore, with buprenorphine there is a decreased risk of abuse, addiction, and side effects compared with other opioids. Buprenorphine was approved for use in the United States for the treatment of opioid dependence in 2002. **Methods:** National estimates of Emergency Department (ED) visits involving buprenorphine were analyzed using data from the 2005 to 2011 Drug Abuse Warning Network (DAWN). The ED visits analyzed included nonmedical use, seeking detoxification/treatment services and adverse reactions involving buprenorphine. **Results:** ED visits involving buprenorphine increased substantially from an estimated 3,161 in 2005 to 30,135 visits in 2010 as availability of the drug increased. Buprenorphine-related ED visits involving nonmedical use of pharmaceuticals increased 255% from 2006 to 2010, with 4,440 visits to 15,778 visits, respectively. In 2010, 52% (15,778 visits) of buprenorphine-related ED visits were classified as nonmedical use of pharmaceuticals, 24% (7,372 visits) were by patients seeking detoxification or substance abuse treatment, and 13% (4,017 visits) were attributed to adverse reactions. In 2010, additional drugs were involved in 59% of buprenorphine-related ED visits involving nonmedical use of pharmaceuticals. **Conclusion:** Findings in this report show significant growth in the number of ED visits involving buprenorphine at the same time that there was an increase in its availability for treatment of opioid dependence. These data show that buprenorphine is sometimes used nonmedically, resulting in health events that require acute treatment in the ED. Buprenorphine use can be risky for individuals who are not opioid dependent because its effects are similar to other opioids (although usually more mild), leading to injuries and other health consequences. Additionally, dangerous effects can occur if buprenorphine is combined with certain other drugs, including benzodiazepines.

Key Words: buprenorphine, opioids addiction, treatment, Drug Abuse Warning Network, DAWN

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KEYWORDS

Short Report, Emergency Department Data, 2005, 2006, 2007, 2008, 2009, 2010, Public Health Professionals, Regulators, Adverse Reaction, Nonmedical Use, Drug Use Trends, Alcohol, Alprazolam, Benzodiazepines, Buprenorphine, Cocaine, Heroin, Marijuana, All US States Only

The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA's mission is to reduce the impact of substance abuse and mental illness on America's communities.

The Drug Abuse Warning Network (DAWN) was a public health surveillance system that monitors drug-related morbidity and mortality. DAWN used a probability sample of hospitals to produce estimates of drug-related emergency department (ED) visits for the United States and selected metropolitan areas annually. DAWN also produced annual profiles of drug-related deaths reviewed by medical examiners or coroners in selected metropolitan areas and States.

Any ED visit related to recent drug use was included in DAWN. All types of drugs - licit and illicit - were covered. Alcohol involvement was documented for patients of all ages if it occurred with another drug. Alcohol was considered an illicit drug for minors and is documented even if no other drug was involved. The classification of drugs used in DAWN was derived from the Multum Lexicon, copyright 2012 Lexi-Comp, Inc., and/or Cerner Multum, Inc. The Multum Licensing Agreement governing use of the Lexicon can be found at <http://www.samhsa.gov/data/emergency-department-data-dawn>.

DAWN is one of three major surveys conducted by SAMHSA's Center for Behavioral Health Statistics and Quality (CBHSQ). For more information on other CBHSQ surveys, go to <http://www.samhsa.gov/data/>. SAMHSA contracted with Westat (Rockville, MD) and RTI International (Research Triangle Park, NC) to operate the DAWN system and produce publications. For publications and additional information about DAWN, go to <http://www.samhsa.gov/data/emergency-department-data-dawn>.



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